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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/602,747	06/24/2003	Laura A. Bedzyk	CL1686USDIV	9974

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EXAMINER

MARVICH, MARIA

ART UNIT	PAPER NUMBER
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1636

DATE MAILED: 07/14/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

SM.

Office Action Summary	Application No. 10/602,747	Applicant(s) BEDZYK ET AL	
	Examiner Maria B Marvich, PhD	Art Unit 1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 24 June 2003.
 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-4, 8, 9 and 14-16 is/are pending in the application.
 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
 5) ☐ Claim(s) _____ is/are allowed.
 6) ☒ Claim(s) 1-4, 8, 9 and 14 is/are rejected.
 7) ☒ Claim(s) 15 and 16 is/are objected to.
 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 a) ☐ All b) ☐ Some * c) ☐ None of:
 1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
 * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

In a preliminary amendment filed 6/24/03, claims 5-7, 10-13 and 17-28 have been cancelled. Claims 1, 2, 4, 8, 9, 15 and 16 have been amended. Claims 1-4, 8, 9 and 14-16 are pending in the application.

Information Disclosure Statement

An IDS filed 6/24/03 has been identified and the documents considered. The signed and initialed PTO Form 1449 has been mailed with this action.

Claim Objections

Claims 15 and 16 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim cannot depend from a multiple dependent claim. See MPEP § 608.01(n). Accordingly, the claims have not been further treated on the merits.

Claims 2 and 4 are objected to because of the following informalities: in claim 2, line 11, "from" is misspelled as "form". In claim 4, line 3, there are two spaces between the word "as" and the word "set". Appropriate correction is required.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground

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provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-4, 8-9 and 14 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-4, 8-9 and 14 of copending Application No. 10/275,191. Although the conflicting claims are not identical, they are not patentably distinct from each other because 1-4, 8-9 and 14 of the copending application anticipates claims 1-4, 8-9 and 14 of the instant application. Claims 1-4, 8-9 and 14 fall entirely within the scope of 1-4, 8-9 and 14 of the instant application. Specifically, the copending claims and the claim of the instant application recite a method of expressing a coding region of interest using the promoter from the *acoABCL* gene.

Additionally, if a patent resulting from the instant claims was issued and transferred to an assignee different from the assignee holding a patent from 10/275,191, then two different assignees would hold a patent to the claimed invention of 10/275,191, and thus improperly there would be possible harassment by multiple assignees.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

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Claims 1-3, 8 and 14 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The instant claims recite a method for the expression of a coding sequence using a promoter region of *yvaWXY* or homologues thereof.

The written description requirement for genus claims may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with known or disclosed correlations between function and structure, or by a combination of such characteristics sufficient to show that the applicant was in possession of the claimed genus.

In the instant case, the specification teaches the identification of genes that are expressed in response to stimuli such as oxygen depletion. The promoter that drives expression of the *Bacillus yvaWXY* gene was identified by high throughput analysis of genes induced upon oxygen depletion (page 18, line 16-19). The nucleotide sequence of *yvaWXY* is contained in SEQ ID NOs 8, 9 and 10 and prophetic and generic stringency conditions for the isolation of homologues are also provided (page 9, line 32). However, applicants do not disclose any homologues of *yvaWXY* or a correlation between the structure of *yvaWXY* and its ability to drive expression under conditions of oxygen depletion. Given the diversity of homologues of the *yvaWXY* promoter and the uncertainty of the activity of any homologue of the *yvaWXY* promoter to be

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effective in driving gene expression, it must be considered that any promoter homologue must be empirically determined. In an unpredictable art, the disclosure of one species would not represent to the skilled artisan a representative number of species sufficient to show applicants were in possession of claimed genus.

Claim 14 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The test of enablement is whether one skilled in the art could make and use the claimed invention from the disclosures in the patent coupled with information known in the art without undue experimentation (*United States v. Telectronics, Inc.*, 8 USPQ2d 1217 (Fed. Cir. 1988)). Whether undue experimentation is required is not based on a single factor but is rather a conclusion reached by weighing many factors (See *Ex parte Forman*, 230 USPQ 546 (Bd. Pat. App. & Inter, 1986) and *In re Wands*, 8USPQ2d 1400 (Fed. Cir. 1988); these factors include the following:

1) **Nature of invention.** The invention recites a method for the expression of a chimeric gene comprised of a promoter and a coding sequence. cDNA microarray techniques that allow identification of genes that are differentially regulated under various stresses and environmental conditions were used to identify promoters to be used for protein production at stationary phase such as the promoter driving expression of the *yvaWXY* gene obtained from *Bacillus*. The instant invention utilizes disciplines of molecular biology and cell culture.

2) **Scope of the invention.** According to claim 14, the expression of the chimeric gene is down regulated at T0 of the stationary phase. The specification discloses that gene expression under the control of *yvaWXY* is induced at stationary phase, therefore the limitation that the chimeric gene be down regulated at T0 complicates the instant method.

3) **Number of working examples and guidance.** The specification does not teach how to down-regulate genes at T0 of stationary phase that are under control of *yvaWXY*. Table 1 discloses that *yvaWXY* is up regulated in response to oxygen depletion in log phase or in the presence of oxygen in stationary phase (Table 1). Furthermore, applicants teach that “reaching T0 of stationary phase under aerobic conditions was sufficient to up regulate the genes” including *yvaWXY* (page 18, line 27-35).

4) **State of Art.** Previously, *Bacillus* was thought to only grown in aerobic conditions (Nakano et al, 1997; applicant provided). Identification and characterization of anaerobic growth pathway in *Bacillus* has revealed several genes that are involved in anaerobic growth conditions. Subsequently it was found that in aerobic growth conditions, cells grow increasing biomass. Upon entry of stationary phase, the cells can be induced to produce protein by induction of genes associated with increased expression upon anaerobic conditions or stationary growth phase. Traditionally, *E. coli* cells have been used for large-scale production of proteins. Isolation and characterization of *yvaWXY* was previously unknown in the art and therefore, methods for its use in protein production are unknown.

5) **Unpredictability of the art.** The art of the instant invention is basically predictable as most components of the invention are built upon well-developed skills. For example, high throughput screening for the identification of genes induced in response to stimuli, protein

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production in *Bacillus*, cloning of promoters and coding regions are well developed skills of the art. It is unpredictable that following the method steps of the instant invention, expression of a chimeric gene under control of *yvaWXY* would be down regulated at TO of the stationary phase. The specification teaches that upon “reaching TO of stationary phase under aerobic conditions was sufficient to up regulate the genes” under control of the promoter *yvaWXY*.

6) **Summary.** The invention recites a method for the expression of a chimeric gene comprised of a promoter and a coding sequence. The unpredictability of using the claimed invention for down-regulation at TO of the stationary phase is accentuated due to the lack of methods or processes for down-regulation of chimeric gene expression provided in the instant specification.

In view of predictability of the art to which the invention pertains and the lack of: undue experimentation would be required to practice the claimed methods with reasonable expectation of success, absent a specific and detailed description in the specification. Given the above analysis of the factors which the courts have determined are critical in determining whether a claimed invention is enabled, it must be concluded that the skilled artisan would have had to have conducted undue unpredictable experimentation in order to practice the claimed invention.

Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

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Claims 1-4, 8-9 and 14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 2 and 8 are vague and indefinite in that the metes and bounds of "the nucleic acid fragment comprising the promoter region of a *Bacillus* gene is *yvaWXY*" are unclear. It is unclear how a fragment comprising a promoter region can be a gene.

Conclusion

Claims 15-16 are objected to as improper multiple dependents.

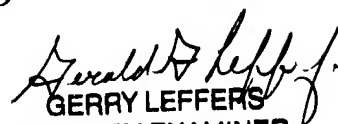
Claims 1-4, 8-9 and 14 are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maria B Marvich, PhD whose telephone number is (571)-272-0774. The examiner can normally be reached on M-F (6:30-3:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, PhD can be reached on (571)-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Maria B Marvich, PhD
Examiner
Art Unit 1636


GERRY LEFFERS
PRIMARY EXAMINER

July 7, 2004